PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 21044-41-1PC	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US03/27523	International filing date (*day/month/year*) 02 September 2003 (02.09.2003)	(Earliest) Priority Date (*day/month/year*) 30 August 2002 (30.08.2002)
Applicant RIGEL PHARMACEUTICALS INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
   ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
   ☒ contained in the international application in written form.
   ☒ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ **Certain claims were found unsearchable** (See Box I).
3. ☒ **Unity of invention is lacking** (See Box II).
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1
   ☐ as suggested by the applicant. ☐ None of the figures
   ☐ because the applicant failed to suggest a figure.
   ☒ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

national application No.
CT/US03/27523

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-3, 5-6, 16, 18, 20-32

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/27523

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12P 21/06, 15/00, 5/00, 15/63; C07H 21/02, 21/04
US CL : 435/69.1, 320.2, 325, 455, 375; 536/23.1, 23.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/69.1, 320.2, 325, 455, 375; 536/23.1, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ALESSI P. et al. Molecular targeting of angiogenesis Biochimica et Biophysica Acta. March 2004, Vol 1654, pages 39-49, see entire document.	1-3, 5-6, 16, 18 and 20-32
A	Database GenEMbl on GenCore. AN:BC025358, November 2003, STRAUSBERG RL et al. Homo sapiens ATP-binding cassette, sub-family D (ALD), member1, mRNA(cDNA clone MGC:39449 IMAGE:4907640), complete cds. see nucleotide sequence which matches SEQ ID NO:3 of instant application.	1-3, 5-6, 16, 18 and 20-32

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
22 July 2004 (22.07.2004)

Date of mailing of the international search report
08 OCT 2004

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
Sumesh Kaushal Ph.D.
Telephone No. 703-308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Claim(s) 1-3, 5-6, 16, 18, 20-32 drawn to a method of identifying a compound that modulate angiogenesis, the method comprises contacting the compound with a nucleic acid sequence that hybridizes to the nucleic acid sequence selected from Group : -

1. SEQ ID NO:3,
2. SEQ ID NO:32,
3. SEQ ID NO:43,
4. SEQ ID NO:57,
5. SEQ ID NO:63,
6. SEQ ID NO:68,
7. SEQ ID NO:70,
8. SEQ ID NO:76,
9. SEQ ID NO:81,
10. SEQ ID NO:86,
11. SEQ ID NO:89,
12. SEQ ID NO:120,
13. SEQ ID NO:128,
14. SEQ ID NO:139,
15. SEQ ID NO:153,
16. SEQ ID NO:163,
17. SEQ ID NO:165,
18. SEQ ID NO:169,
19. SEQ ID NO:171,
20. SEQ ID NO:173,
21. SEQ ID NO:175,
22. SEQ ID NO:183,
23. SEQ ID NO:202,
24. SEQ ID NO:210,
25. SEQ ID NO:218,
26. SEQ ID NO:227,
27. SEQ ID NO:232,
28. SEQ ID NO:248,
29. SEQ ID NO:274,
30. SEQ ID NO:285,
31. SEQ ID NO:286,
32. SEQ ID NO:297,
33. SEQ ID NO:307,
34. SEQ ID NO:308,
35. SEQ ID NO:317,
36. SEQ ID NO:318,
37. SEQ ID NO:320,
38. SEQ ID NO:323,
39. SEQ ID NO:324,
40. SEQ ID NO:329,
41. SEQ ID NO:330,
42. SEQ ID NO:340,
43. SEQ ID NO:351,
44. SEQ ID NO:365,
45. SEQ ID NO:377,

46. SEQ ID NO:384,
47. SEQ ID NO:406,
48. SEQ ID NO:408,
49. SEQ ID NO:419,
50. SEQ ID NO:421,
51. SEQ ID NO:428,
52. SEQ ID NO:437,
53. SEQ ID NO:439
54. SEQ ID NO:445,
55. SEQ ID NO:456,
56. SEQ ID NO:462,
57. SEQ ID NO:481,
58. SEQ ID NO:484,
59. SEQ ID NO:493,
60. SEQ ID NO:496,
61. SEQ ID NO:498,
62. SEQ ID NO:519

Claims 1-17, 19-24 25-32 drawn to a method of identifying a compound that modulate angiogenesis, the method comprises contacting the compound with a polypeptide encoded by a nuclei acid sequence that hybridizes to the nucleic acid sequence selected from Group : -

63. SEQ ID NO:4,
64. SEQ ID NO:33,
65. SEQ ID NO:44,
66. SEQ ID NO:58,
67. SEQ ID NO:64,
68. SEQ ID NO:69,
69. SEQ ID NO:71,
70. SEQ ID NO:77,
71. SEQ ID NO:82,
72. SEQ ID NO:87,
73. SEQ ID NO:90,
74. SEQ ID NO:121,
75. SEQ ID NO:129,
76. SEQ ID NO:140,
77. SEQ ID NO:154,
78. SEQ ID NO:164,
79. SEQ ID NO:170,
80. SEQ ID NO:172,
81. SEQ ID NO:174,
82. SEQ ID NO:176,
83. SEQ ID NO:184,
84. SEQ ID NO:203,
85. SEQ ID NO:287,
86. SEQ ID NO:298,
87. SEQ ID NO:309,
88. SEQ ID NO:319,
89. SEQ ID NO:325,
90. SEQ ID NO:331,
91. SEQ ID NO:341,
92. SEQ ID NO:352,
93. SEQ ID NO:366,
94. SEQ ID NO:378,
95. SEQ ID NO:385,
96. SEQ ID NO:407,
97. SEQ ID NO:409,
98. SEQ ID NO:420,
99. SEQ ID NO:429,
100. SEQ ID NO:438,
101. SEQ ID NO:440,
102. SEQ ID NO:446,
103. SEQ ID NO:457,

104. SEQ ID NO:463,
105. SEQ ID NO:482,
106. SEQ ID NO:485,
107. SEQ ID NO:494,
108. SEQ ID NO:497,
109. SEQ ID NO:499,
110. SEQ ID NO:520

Claims 33, drawn to a method of modulating angiogenesis in a subject by administering a therapeutic effective amount of a polypeptide encoded by a nucleic acid sequence which hybridizes to the nucleic acid sequence selected from Group : -

111. SEQ ID NO:63,
112. SEQ ID NO:76,
113. SEQ ID NO:81,
114. SEQ ID NO:86,
115. SEQ ID NO:89,
116. SEQ ID NO:120,
117. SEQ ID NO:128,
118. SEQ ID NO:165,
119. SEQ ID NO:183,
120. SEQ ID NO:202,
121. SEQ ID NO:218,
122. SEQ ID NO:232,
123. SEQ ID NO:274,
124. SEQ ID NO:285,
125. SEQ ID NO:286,
126. SEQ ID NO:297,
127. SEQ ID NO:317,
128. SEQ ID NO:318,
129. SEQ ID NO:320,
130. SEQ ID NO:323,
131. SEQ ID NO:324,
132. SEQ ID NO:340,
133. SEQ ID NO:377,
134. SEQ ID NO:384,
135. SEQ ID NO:406,
136. SEQ ID NO:408,
137. SEQ ID NO:439
138. SEQ ID NO:445,
139. SEQ ID NO:456,
140. SEQ ID NO:481,
141. SEQ ID NO:484,
142. SEQ ID NO:493,
143. SEQ ID NO:496,
144. SEQ ID NO:498.

Claims 34, drawn to a method of modulating angiogenesis in a subject by administering a therapeutic effective amount of a nucleic acid sequence which hybridizes to the nucleic acid sequence selected from Group : -

145. SEQ ID NO:3,
146. SEQ ID NO:32,
147. SEQ ID NO:43,
148. SEQ ID NO:57,
149. SEQ ID NO:63,
150. SEQ ID NO:68,
151. SEQ ID NO:70,
152. SEQ ID NO:76,
153. SEQ ID NO:81,
154. SEQ ID NO:86,
155. SEQ ID NO:89,
156. SEQ ID NO:120,
157. SEQ ID NO:128,
158. SEQ ID NO:139,
159. SEQ ID NO:153,

160. SEQ ID NO:163,
161. SEQ ID NO:165,
162. SEQ ID NO:169,
163. SEQ ID NO:171,
164. SEQ ID NO:173,
165. SEQ ID NO:175,
166. SEQ ID NO:183,
167. SEQ ID NO:202,
168. SEQ ID NO:210,
169. SEQ ID NO:218,
170. SEQ ID NO:227,
171. SEQ ID NO:232,
172. SEQ ID NO:248,
173. SEQ ID NO:274,
174. SEQ ID NO:285,
175. SEQ ID NO:286,
176. SEQ ID NO:297,
177. SEQ ID NO:307,
178. SEQ ID NO:308,
179. SEQ ID NO:317,
180. SEQ ID NO:318,
181. SEQ ID NO:320,
182. SEQ ID NO:323,
183. SEQ ID NO:324,
184. SEQ ID NO:329,
185. SEQ ID NO:330,
186. SEQ ID NO:340,
187. SEQ ID NO:351,
188. SEQ ID NO:365,
189. SEQ ID NO:377,
190. SEQ ID NO:384,
191. SEQ ID NO:406,
192. SEQ ID NO:408,
193. SEQ ID NO:419,
194. SEQ ID NO:421,
195. SEQ ID NO:428,
196. SEQ ID NO:437,
197. SEQ ID NO:439
198. SEQ ID NO:445,
199. SEQ ID NO:456,
200. SEQ ID NO:462,
201. SEQ ID NO:481,
202. SEQ ID NO:484,
203. SEQ ID NO:493,
204. SEQ ID NO:496,
205. SEQ ID NO:498,
206. SEQ ID NO:519

Claims 35-36, drawn to an isolated nucleic acid sequences or variants thereof selected from Group : -

207. SEQ ID NO:165,
208. SEQ ID NO:202,
209. SEQ ID NO:210,
210. SEQ ID NO:218,
211. SEQ ID NO:227,
212. SEQ ID NO:232,
213. SEQ ID NO:248,
214. SEQ ID NO:274,
215. SEQ ID NO:285,
216. SEQ ID NO:286,
217. SEQ ID NO:297,
218. SEQ ID NO:307,
219. SEQ ID NO:308,

220. SEQ ID NO:317,
221. SEQ ID NO:318,
222. SEQ ID NO:320,
223. SEQ ID NO:323,
224. SEQ ID NO:324,
225. SEQ ID NO:329,
226. SEQ ID NO:330.

Claims 37, drawn to an isolated polypeptide selected from Group : -
227. SEQ ID NO:287,
228. SEQ ID NO:298,
229. SEQ ID NO:309,
230. SEQ ID NO:319,
231. SEQ ID NO:325,
232. SEQ ID NO:331.

The inventions listed as Groups 1-232 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Groups 1-62 are compounds that interacts with nucleic acid sequences.
The special technical feature of Groups 63-110 are compounds that interacts with polypeptides.
The special technical feature of Groups 64-144 is protein therapy.
The special technical feature of Groups 145-206 is gene therapy.
The special technical feature of Groups 207-226 are nucleic acid sequences.
The special technical feature of Groups 227-232 are polypeptide sequences.

This international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the reasons indicated below:

According to the guidelines in Section (9(i)(a) of Annex B of the PCT Administrative instruction, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed sequences) the Markush group shall be regarded as being of similar nature when

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e, a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all
alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant application claims multiple polynucleotide and polypeptide sequences, which are considered to lack unity because:

These sequences do not meet the criteria of (A), common property or activity or (B)(2) art recognized class of compounds. Each sequence behave in a different way in the context of the claimed invention. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved.

Further, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the nucleotide and protein sequences is lacking and each sequence claimed is considered to constitute a special technical feature.

Continuation of B. FIELDS SEARCHED Item 3:
Databases: Medline, Caplus, STIC sequcne database.
Search terms: Angiogenesis, ATP-binding cassette, screening, method, nucleic acid seqcnes of SEQ ID NO:3.